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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,925	07/11/2001	Avi Ashkenazi	10466/86	1358

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	16

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.	Applicant(s)
09/903,925	Ashkenazi et al.
Examiner	**Art Unit**
Fozia Hamud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 11, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *39-43* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *39-43* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Office Action

1a. Receipt of Applicants' arguments and amendments filed in Paper No.13 on 07 February 2003 is acknowledged. Claim 44 is canceled and claim 39 is amended. Thus claims 39-43 are pending and under consideration.

1b. Receipt of Applicant's declaration under 37 C.F.R §1.132, filed in Paper No.12, 07 February 2003, in Paper No.12 is also acknowledged.

2. The following previous objections and rejections are withdrawn in light of Applicants amendment filed in Paper No.13, 02/07/03:

(I) The objection to the specification for containing an embedded hyperlink.

Priority

Applicants contend that the claimed subject matter was disclosed in the international PCT application PCT/US99/30095, filed 16 December 1999 (WO 00/37640), which claims priority to US provisional application No:60/113,296 filed on 22 December 1998, therefore, the present application is entitled to the filing date of 22 December 1998.

This argument is not found persuasive, because, the subject matter defined in this application is not supported by the disclosure in the international application PCT/US99/30095, filed 16 December 1999 or in the provisional application No:60/113,296 filed on 22 December 1998, since these prior applications do not provide a specific and substantial asserted utility or a well established utility for the claimed invention. Furthermore, Applicants state that the subject of the instant Application was disclosed was disclosed in the international PCT application PCT/US99/30095,

filed 16 December 1999 (WO 00/37640, however, Applicants do not state whether the claimed subject matter was also disclosed in the 60/113,296 application, field on 22 December 1998. Accordingly, the subject matter defined in claims 39-43 is afforded an effective filing date of 07/11/2001 which is the filing date of the current application.

Claim Rejections under 35 U.S.C. §101/112:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3a. Claims 39-43 stand rejected under 35 U.S.C. §101 for reasons of record set forth in the office action mailed on 10 September 2002 in Paper NO:11, pages 3-4.

Applicants argue that they have provided specific and substantial utility for the claimed inventions. Applicants submit that the gene amplification data provided in the present application are sufficient to establish a specific, substantial and credible utility for the PRO343 polypeptide. Applicants argue that gene amplification is essential mechanism for oncogene activation, and that it is well known in the art that gene amplification occurs in most solid tumors and generally is associated with poor prognosis. Applicants cite Example 92 of the instant application which demonstrates that PRO343 DNA was 2-9 folds higher in primary lung tumors and in primary colon tumors compared to DNA isolated from normal controls. Applicants submit a Declaration by Audrey Goddard and also submit references regarding gene amplification studies.

Applicants' arguments have been fully considered, but are not deemed persuasive. Instant specification discloses gene amplification assay utilizing genomic DNA samples from primary

tumors and tumor cell lines which demonstrates an approximately 2-9 fold amplification of DNA sequences in lung and colon tumors compared to normal controls. Thus, polynucleotide encoding PRO343 may be used to detect cancer cells due to increased copy number, thus establishing an asserted utility that is specific, substantial and credible for the DNA. However, the increased copy number of DNA does not provide a readily apparent use for the polypeptide, because there is no information regarding the level of expression, an activity, or a role in cancer for the polypeptide or the claimed antibody which binds to said polypeptide.

The data in the instant specification (and reviewed in the Declaration) show that gene copy number is increased in certain tumor tissue samples, however, it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased protein expression, such that the antibodies would be useful diagnostically or as target for cancer drug development. For example, Pennica et al, (1998, PNAS USA 95:14717-14722, Exhibit D of the Declaration) discloses that, "An analysis of WISP-1 gene amplification in human colon tumors showed a correlation between DNA amplification and over expression, whereas, over expression of WISP-3 RNA was seen in the absence of DNA amplification. In contract, WISP-2 DNA was amplified in the colon tumors, but mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient", see page 14722, second paragraph of column 1; pages 14720-14721. Therefore, the protein levels cannot be accurately predicted from the level of the corresponding gene.

Thus, the PRO343 polypeptide and antibodies that bind to said polypeptide lack a specific or substantial utility, because there is no indication that the polypeptide is increased in the lung or colon tumors compared to normal controls.

3b. Claims 39-43 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the action mailed on 10 September 2002 in Paper NO:11, pages 3-4.

Specifically, the increased copy number of PRO343 DNA in lung and colon tumors, does not provide a readily apparent use for the polypeptide or the antibodies against the polypeptide, because there is no information regarding the level of expression, an activity, or a role in cancer for the PRO343 polypeptide or antibodies which bind to said polypeptide, one of ordinary skill in the art would not know how to use the claimed antibody..

37 CFR 1.132 Declaration

4. The declaration under 37 C.F.R §1.132, filed in Paper No.12, 07 February 2003 is insufficient to overcome the rejection of claims 39-43 based upon 35 U.S.C 101/112.

The Declaration submitted by Dr. Goddard has been fully considered, but is deemed unpersuasive to overcome the rejection of claims 39-43 based upon 35 U.S.C 101/112. Dr. Goddard submits references that describe the gene amplification technique used in the present application and references that attest to the use of this technique in diagnostic and prognostic fashion. Finally, Dr. Goddard states that the gene amplification technique used in the present specification is sensitive enough to detect a 2 fold increase and the a 2 fold increase in gene copy number in a tumor tissue compared to a normal tissue is significant and useful in a diagnostic manner.

Dr. Goddard's assertion that gene amplification is sensitive enough to detect a 2 fold increase and the a 2 fold increase in gene copy number in a tumor tissue compared to a normal tissue is significant and useful in a diagnostic manner, is correct. However, instant specification does not demonstrate that the increased copy number of PRO343 DNA in lung and colon tumors, leads to an increased expression of PRO343 polypeptide in these tumors. Therefore, since Applicants do not provide information regarding the level of expression, an activity, or a role in cancer or any other disease for the PRO343 polypeptide or the claimed antibody which binds to said polypeptide, both the polypeptide and the antibody lack a substantial utility or well established utility, (see section 3a of this office action).

Claim Rejections - 35 U.S.C. §102(b)

5. The rejection of c claims 39-40, 42-43 are made under U.S.C. § 102 (b) as being anticipated by Amrad Operations Pty. Ltd (WO 98/36054; published 20 August 1998) is maintained for reasons of record set forth in the office action mailed on 10 September 2002 in Paper NO:11, page 5.

Applicants argue that the protein disclosed by Amrad Operations Pty. Ltd and the polypeptide with the amino acid sequence set forth in SEQ ID N O:263, of the instant application share 85.48% overall identity and refer to an attachment. Applicants contend that the claims as currently amended concern an antibody that binds specifically to the polypeptide of SEQ ID NO:263, as such they do not bind to a polypeptide that has about 85% overall sequence identity with SEQ ID NO:263.

These arguments have been fully considered but are not deemed persuasive. The alignment attachment Applicants have referred to is not attached to this response. However, whether the polypeptide of SEQ ID NO:263 and the polypeptide disclosed in the WO 98/36054 reference share

85% or 86.5% (as the search for SEQ ID NO:263 conducted by the USPTO revealed) is irrelevant, because an antibody that binds with SEQ ID NO:263 would also bind to a polypeptide that shares 85% identity, because the similarities between the polypeptides are greater than their differences. The recitation of "specifically binds..." in claim 39 does not overcome this rejection, because the it is unclear what "specifically binds" means, does it mean that the claimed antibody only binds to SEQ ID NO:263 and does not bind any other protein? If this is the case, then it is not possible to produce an antibody that binds only to SEQ ID NO:263, because the specification does not give a written description or the guidance needed to produce an antibody which binds only to SEQ ID NO:263 and does not cross react with any other protein. The specification does not teach whether there are unique epitopes found in SEQ ID NO:263 that would enable the production of an antibody that would only bind to SEQ ID NO:263. The claimed antibody would be expected to cross react to the polypeptide disclosed in WO 98/36054 as well as to the polypeptide of SEQ ID NO:263, because of the high percent homology between the two polypeptides. Antibodies bind to epitopes and an epitope need to comprise only 6 amino acid residues, therefore, since the two polypeptides share 271 identical amino acid residues, the claimed antibody would bind to both polypeptides. The fact that the polypeptide of SEQ ID NO:263 comprises 46 more amino acid residues, does not exclude for the claimed antibody from binding to the polypeptide of the reference.

Claim Rejections - 35 U.S.C. §103

6. Claims 39 and 41 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Amrad Operations Pty. Ltd. (WO 98/36054) in view of Carter et al. (U.S. Patent 5,821,337), for reasons of record set forth in the office action mailed on 10 September 2002 in Paper NO:11, pages 6-7.

Applicants argue that since Amrad Operations Pty. Ltd. (WO 98/36054) reference does not anticipate the rejected claims, then its combination with Carter et al, does not make obvious the invention of the pending claims, because Carter et al is applied only to show that humanized antibodies were known in the art at the effective filing date of the present application.

This argument is not found persuasive, because Amrad Operations Pty. Ltd. (WO 98/36054) reference discloses the claimed antibody (see section 5 of this office action), and it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the antibody taught by Amrad Operations Pty. Ltd, by humanizing said antibody by following the teachings of Carter et al. Thus the combination of the two references, renders the invention recited in claims 39 and 41 obvious.

Conclusion

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE?MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Thursday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
15 April 2003

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